

Allometric scaling and maximum efficiency in physiological eigen time

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General optimization results from physics indicate that maximum efficiency of a process, in the sense of minimum overall entropy production, is achieved when the rate of entropy production is constant over time, however not in ordinary clock time but on an, in general varying, “eigen time” scale, intrinsic to the system. We identify the eigen time of a biological system with “physiological time,” which generally scales with the $1/4$ power of body mass, $M^{1/4}$, over a vast range of species. Since it is equally well established that metabolic rate scales as $M^{3/4}$, it follows that organisms produce entropy at the same intrinsic rate, fulfilling a necessary condition for maximum efficiency, and are all, furthermore, equally efficient on the physiological eigen time scale.

Maximum efficiency is an attractive design principle for biological systems. It has been argued for on evolutionary (1) as well as thermodynamic grounds (see e.g., refs. 2–4). Recently there have been several attempts (5–8) to derive general allometric scaling laws (9–11) from just such a principle of maximum efficiency. According to these laws, empirically valid over a vast range of species from microorganisms to the largest mammals, various biological times (e.g., lifespan and the time between heartbeats) scale with body mass to the $1/4$ power, and resting metabolic rate scales with body mass to the $3/4$ power. Most of the arguments leading from maximum efficiency to the scaling laws suffer, however, from internal inconsistencies, a disregard for restrictive conditions on the validity of theoretical results, or some other failing. A notable exception to this trend is Bejan’s constructal design principle, which results in an optimal geometric form for which dissipation turns out to scale with the $3/4$ power of size (8).

The traditional argument, recently (1, 5, 7) as well as in the past (12), for maximum efficiency of biological systems rests on the statement “... natural selection is responsible for ... the trend toward optimal efficiency in organisms” (1). It is evidently obvious, then, that the organism with the highest efficiency is the fittest. It is also tempting to argue (2–4, 13) that the classical formulation of nonequilibrium thermodynamics of Onsager (14, 15) and Onsager and Machlup (16, 17) [although often attributed to Prigogine and Wiame (18)] implies maximum efficiency. These authors showed that in a certain class of non-equilibrium stationary states, entropy production rate is at a minimum. Because living systems are nonequilibrium systems, their stationary states are maximally efficient, or so it is argued.

All these arguments, however, are doomed to failure. (i) Although the criticism that the “survival of the fittest” argument is tautological may be argued to have been rebutted, there still remain significant questions regarding the proper concept of fitness [ref. 19; see R. L. Millstein (2001) http://philsci-archive.pitt.edu/documents/disk0/00/00/02/10/PITT-PHIL-SCI00000210-00/Millstein_Evolution3.pdf]. (ii) Onsager’s results are generally valid only in the linear near-equilibrium regime, whereas the living state is far from equilibrium and nonlinear (20–22). (iii) When it is argued on evolutionary grounds that efficiency is maximum to derive the universal biological allometric scaling laws (9, 10), the argument is typically applied to particular subsystems or processes of the organ-

ism, supply of materials to the organism (5), or hovering and jumping (7), for example. However, when subsystems interact, an optimal system does not imply that all subsystems are optimal; indeed, in general it will not be possible to optimize all subsystems independently without encountering irreconcilable contradictions. (iv) The very allometric scaling laws that are to be derived on the basis of a principle of maximum efficiency predict that loss (inefficiency), in the sense of the rate of energy usage per unit body mass, decreases with increasing body mass (23). One may then naively ask why the body mass of mammalian species ranges over seven orders of magnitude? If maximum efficiency is to be equated with fitness, then larger implies fitter, and only the largest species should have survived.

Obviously, a new line of thought is required to reconcile the biological facts. In this paper we turn the question around and ask not whether we can derive the scaling laws from efficiency considerations, but rather what these empirical scaling laws tell us about efficiency. In this light the allometric scaling laws, as seen below, imply a constant metabolic rate for organisms, not, however, as seen on the time scale of an outside observer or measured in seconds by some physical clock, but in what Schmidt-Nielsen (10) has called “physiological time.” Note that this new time scale is not simply a linear transformation to new units, which would have made the exercise shallow. The new time scale is variable and depends on the rate of the interior processes of the organism. We argue here that physiological time is equivalent to thermodynamic “eigen time” (24), or “intrinsic time” if you wish, which is based on the instantaneous relaxation time of the system itself. As a consequence, biological systems fulfill a necessary condition for maximum efficiency in the sense of minimum total entropy production, namely a constant rate of entropy production, again not in clock time but in eigen time (24, 25). Furthermore, on the physiological eigen time scale, organisms not only fulfill a necessary condition for maximum efficiency, they are also all equally efficient.

Eigen Time

The general conditions necessary for maximum efficiency, in the sense of minimum overall entropy production, in arbitrary systems have recently been derived by Andresen and Gordon (24) and Spirkel and Ries (25). Andresen and Gordon (24) used the concept of thermodynamic geometry (26), whereas Spirkel and Ries (25) used the calculus of variations. Both groups found that in general these conditions depend on the detailed dynamics of the system and that entropy production will be minimum for only certain paths among all those available to the system. They also found that if the dynamics of the system is such that the relation between the generalized forces and the generalized rates these forces drive is linear in the rates, then a necessary condition for minimum total entropy production is that the rate of entropy

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production be constant (27). Note that even though this restriction is severe and cannot be expected to be valid in general for biological systems, it does not imply that one is operating in the linear near-equilibrium regime, since nonlinearities may be present in the dependence of the force–rate relation on the state of the system.

The results just cited are for clock time; i.e., the rate of entropy production is that seen by an observer outside the system. Andresen and Gordon (24) went on to show that if the rates are normalized to the intrinsic time scale of the system, based on its instantaneous relaxation time (which may change with time as seen by an outside observer) (28), then the restriction to linear force–rate dynamics no longer applies, and the general necessary condition for minimum overall entropy production is a constant rate of entropy production on this intrinsic time scale, independent of any condition on linearities or any other simplifying assumptions about the dynamics. In other words, on the internal time scale of the system itself, referred to as *eigen* time, equal time intervals produce equal changes in entropy. Or put still another way, as the system perceives itself, minimum entropy production requires a constant rate of entropy production. This distinction between time as perceived by an outside observer and as perceived by the system itself is not as unusual as it may seem. It is well known in the theory of relativity and is the basis of the twin paradox (see, e.g., refs. 29 and 30).

Let us consider a simple example to illustrate the concepts of optimal path and eigen time, an ideal damped spring with spring constant κ and friction coefficient β . Ordinarily the spring would obey the natural differential equation $dx/dt = -(\kappa/\beta)x$. The resulting position x and rate of entropy production σ as function of clock time t are then $x = x_0 e^{-(\kappa/\beta)t}$ and $\sigma = \beta(dx/dt)^2 = (\kappa^2/\beta)x_0^2 e^{-2(\kappa/\beta)t}$. This natural path, however, is not the one producing the least entropy (i.e., it is not optimal), and the entropy production rate is not constant. The optimized path calls for a constant speed $v = dx/dt$, which in turn implies a constant rate of entropy production, $\sigma = \beta v^2$. Such an optimal path requires an outside controlling agent to implement the required $x(t)$. For this system the eigen time $\tau = t/\varepsilon$, where ε is the instantaneous relaxation time of the system, is simply $\tau = (\kappa/\beta)t$.

For more complicated systems ε will vary along the path, and correspondingly τ will not be a linear function of t . A slight variation of the example above, using a quadratic spring, yields the differential equation $dx/dt = -(\kappa/\beta)x^2$ and thus the natural time evolution $x = 1/(1 + (\kappa/\beta)t)$. Again, this is different from the optimal path that requires a constant rate of entropy production. For this system the eigen time is $\tau = t/\varepsilon = (\kappa/\beta)t$; i.e., it dilates as x increases. Put another way, eigen time τ increases nonlinearly with clock time t : $\tau = (\kappa/\beta)t/(1 + (\kappa/\beta)t)$.

Of course, the systems we are interested in are not described by a single variable, but rather by many. Organisms will in general have very large numbers of variables. Nonetheless, the concept of eigen time is the same as that just illustrated. It is the internal time scale of the system that leads to equal steps in entropy for equal steps in (eigen) time.

Physiological Time

What is the proper eigen time for an organism, and what is the rate of entropy production for the organism in this eigen time? To answer these questions we turn to allometric scaling laws in biological systems, which could be said to belong to the few well established fundamental principles in biology (9–11). Over a stupefying range of body masses M , from unicellular organisms through blue whales, metabolic rate scales as $M^{3/4}$, and characteristic times scale as $M^{1/4}$. Furthermore, the scaling laws appear to be valid not only for animals but also for plants (31) as well as ecosystems (32). There is overwhelming evidence that the time between heartbeats, the time between respirations, the gestation period, even species longevity, all scale as $M^{1/4}$. This scaling of essentially all natural periods with body weight is what

is called “physiological time,” a term coined by Schmidt-Nielsen (10). Note that these scaling laws are not characteristics of an individual organism at a particular instant of time. Rather, they are of the nature of ensemble averages (over a species), and usually taken under resting conditions.

The identical scalings of natural periods imply several constants: the ratio of respiration frequency to heart rate, the ratio of gestation time to longevity, the number of respirations or heartbeats in a lifetime. Indeed, each species lives for roughly the same number of heartbeats or respirations. Whereas each species appears to be different when observed from the outside (clock time), each species’ temporal view of itself is identical. It sees each heart beat, each respiration as the same fraction of its lifespan. Physiological time is thus the intrinsic, inherent time scale of organisms. This is just what is intimated by the concept of eigen time. From these observations we can infer that the physiological time scale $\tau = \tau_0 M^{1/4}$, where τ_0 is a constant, is the eigen time scale for organisms.

As impressive as the scaling of physiological time is that of metabolic rate R , which scales as $M^{3/4}$ over a very wide range of body masses, from unicellular organisms to blue whales, $R = R_0 M^{3/4}$, with R_0 constant over a tremendous range of M . It is important to realize that metabolic rate is a measure independent of physiological time. Although it is tempting to argue that all time dependence eventually boils down to the rate of chemical reactions in the organism and thus metabolic rate, the two time scales have no relationship, just as the frequency of a radio transmitter is unrelated to the frequency of its power supply but is an intrinsic quantity. Only in the hypothetical case that a mechanistic coupling between metabolic (power generation) rate and one of the natural periods can be proven will metabolic rate and physiological time be expressions of the same rate.

For an isothermal system the rate (in clock time) of entropy production can be taken as given by the metabolic rate. Although efficiency is often treated in energetic terms, e.g., metabolic rate, the proper basis for discussion is entropy (see, e.g., refs. 13 and 33), since energy is strictly conserved in any process, whereas entropy always increases—it yields the “arrow of time.” Thermodynamic efficiency based on entropy is also a more general quantifier than an efficiency based on energy, since the maximum of the latter depends on the temperature of the system (through the Carnot efficiency) whereas the maximum entropic efficiency (also sometimes called effectiveness) is always one. However, under isothermal conditions, i.e., particularly in the case of homeotherms, energetic and entropic changes are simply proportional, so changes in one reflect changes in the other. In the more general case where work potential (exergy) may be made useful at several intensities (e.g., heat at different temperatures), the two descriptions are no longer equivalent (34). Thus, we take entropy as the proper measure of efficiency and infer that the rate of entropy production scales with $M^{3/4}$.

Maximum Efficiency

From the scaling of physiological time and that of the rate of entropy production we see that on the physiological time scale τ (e.g., per heartbeat) the rate of metabolism R or the rate of entropy production per unit body mass is constant: $R\tau/M = \tau_0 M^{1/4} R_0 M^{3/4}/M = R_0 \tau_0$. This implies in turn that the total (over the entire lifespan) entropy production per unit body mass is the same for all species, and that the rate of entropy production per unit body mass is constant across species on the physiological eigen time scale. This is nothing but the necessary condition for maximum efficiency in the sense of minimum entropy production derived by Andresen and Gordon (24) and Spirkel and Ries (25). Although this is only a necessary condition, not a sufficient one, it indicates that organisms do indeed operate at maximum efficiency.

Since metabolic rate increases with body mass at a rate less than body mass itself, the rate of entropy production per unit body mass

decreases with increasing mass in clock time; thus the statement that smaller species are energetically less efficient than larger ones (23). On the other hand, note that total energy usage over the entire lifespan of a representative of a particular species is just the product of metabolic rate and longevity (more correctly the integral of metabolic rate with respect to time) and is proportional to body mass ($R\tau = R_0\tau_0M$). Therefore, total energy usage per unit body mass over species lifespan is constant, as is the metabolic rate per unit body mass in physiological time. In this sense, all species are equally efficient on the physiological eigen time scale. It is only when observing organisms from the outside that we see increasing efficiency with increasing body mass.

It is important to keep in mind that the results here do not require exactly $1/4$ power scaling, the origins of which have been the subject of intensive investigation recently (see, e.g., refs. 11 and 35; see also ref. 8). All that is required is that if metabolic rate scales as $M^{1-\alpha}$ then physiological time must scale as M^α . This ensures that the product of the rate of entropy production and eigen time is proportional to M ; maximum efficiency follows. Although the evidence for $1/4$ power scaling is strong, other scalings—e.g., the $1/3$ power scaling expected on geometrical grounds—would equally support the result of maximum efficiency derived here, as long as physiological time would be found to scale appropriately on closer examination.

Note also that if evolution is the omnipotent optimizer that some would maintain, then it is entire organisms that are maximally efficient, not particular processes or organ systems. The condition of maximum efficiency for individual processes or organ systems might even lead to logical conflicts with current physiological knowledge. For example, one could reasonably argue that skeletal muscle should be a maximally efficient mechanical system, but skeletal muscle is also involved in temperature regulation through shivering. For muscle to be optimal in the latter role, it should produce a maximum of heat; i.e., it should be minimally efficient. Muscle cannot be optimal in both of these senses. However, if the organism as a whole is maximally efficient, this does not require that muscle or any other component system is maximally efficient in any one role. Organismal optimal efficiency can thus circumvent apparent conflicts that may arise when attempting to optimize component systems for multiple roles. This would also be consistent with approaches that apparently explain the allometric scaling laws without recourse to energetic arguments (6).

Evolutionary theoretical, including life history theoretical (36), interpretations of these results are best left to specialists in these fields. Nonetheless, a few points are apparent, even if they may border on the speculative. The first is that the efficiency optimization inferred from the scaling laws may not be unique to living systems; it is also found in natural physical systems such as rivers (8), at least as reflected in their structures. Second, as emphasized by Bejan (8), these same sorts of structures are those that often lead to optimal efficiency in man-made systems, especially those dealing with flows. Thus, the allometric scaling laws may be a reflection of a more universal natural law relating to efficiency, and may not be unique to systems arising through biological evolution. In fact, the evolution of man-made and other nonbiological systems seem similar in this regard (8). Third, from a life-history theoretical point of view, it would seem reasonable that the efficiency of an organism is related to its lifespan in such a way that all organisms are equally, and maximally, efficient, each on its own physiological eigen time scale. If a cat had the same lower metabolic rate as the longer lived elephant, it would be hyperefficient; i.e., its rate of entropy production would be lower than it could be and still maintain maximal efficiency. If, on the other hand, the cat would produce entropy at the faster rate of the smaller shrew, this rate would be too large to be maximally efficient. Finally, consistent with the last point, there are indications (31) that growth rate may be adjusted to lifespan in such a way that, again, the conditions for maximum efficiency in the sense of total entropy production are met.

Up to now, the question asked most frequently has concerned the derivation of the allometric scaling laws from a condition of maximum efficiency. Here we have turned the question around, and, instead of asking what a principle of maximum efficiency can tell us about the origins of the universal scaling laws (5, 8), we have asked what the scaling laws can tell us about efficiency. We found that each species is equally efficient in physiological eigen time, and that a necessary condition for maximum efficiency in the sense of minimum entropy production is fulfilled. Thus biological systems may indeed be maximally efficient—not in clock time as seen by an outside observer, but in physiological eigen time, as each species sees itself.

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- Bonner, J. T. & Horn, H. S. (2000) in *Scaling in Biology*, eds. Brown, J. H. & West, G. B. (Oxford Univ. Press, Oxford), pp. 25–35.
- Zotin, A. I. & Zotina, R. S. (1967) *J. Theor. Biol.* **17**, 57–75.
- Wilson, T. A. (1966) *J. Theor. Biol.* **11**, 436–445.
- Dewey, T. G. & Donne, M. D. (1998) *J. Theor. Biol.* **193**, 593–599.
- West, G. B., Brown, J. H. & Enquist, B. J. (1997) *Science* **276**, 122–126.
- Banavar, J. R., Maritan, A. & Rinaldo, A. (1999) *Nature (London)* **399**, 130–132.
- Alexander, R. M. (2000) in *Scaling in Biology*, eds. Brown, J. H. & West, G. B. (Oxford Univ. Press, Oxford), pp. 37–50.
- Bejan, A. (2000) *Shape and Structure, From Engineering to Nature* (Cambridge Univ. Press, Cambridge, U.K.).
- Peters, R. H. (1983) *The Ecological Implications of Body Size* (Cambridge Univ. Press, Cambridge, U.K.).
- Schmidt-Nielsen, K. (1984) *Scaling: Why Is Animal Size So Important?* (Cambridge Univ. Press, Cambridge, U.K.).
- Brown, J. H. & West, G. B., eds. (2000) *Scaling in Biology* (Oxford Univ. Press, Oxford).
- Thompson, D. W. (1917) *On Growth and Form* (Cambridge Univ. Press, Cambridge, U.K.).
- Briedis, D. & Seagrave, R. C. (1984) *J. Theor. Biol.* **110**, 173–193.
- Onsager, L. (1931) *Phys. Rev.* **37**, 405–426.
- Onsager, L. (1931) *Phys. Rev.* **38**, 2265–2279.
- Onsager, L. & Machlup, S. (1953) *Phys. Rev.* **91**, 1505–1512.
- Onsager, L. & Machlup, S. (1953) *Phys. Rev.* **91**, 1512–1515.
- Prigogine, I. & Wiame, J. M. (1946) *Experientia* **2**, 451–453.
- Millstein, R. L. (2002) in *Blackwell Guide to the Philosophy of Science*, eds. Machamer, P. K. & Silberstein, M. (Blackwell, Oxford), pp. 227–251.
- Richardson, I. W. (1969) *Biophys. J.* **9**, 265–267.
- Ulanowicz, R. E. & Hannon, B. M. (1987) *Proc. R. Soc. London Ser. B* **232**, 181–192.
- Aoki, I. (1991) *J. Theor. Biol.* **150**, 215–223.
- West, G. B., Brown, J. H. & Enquist, B. J. (2000) in *Scaling in Biology*, eds. Brown, J. H. & West, G. B. (Oxford Univ. Press, Oxford), pp. 87–112.
- Andresen, B. & Gordon, J. M. (1994) *Phys. Rev. E Stat. Phys. Plasmas Fluids Relat. Interdiscip. Top.* **50**, 4346–4351.
- Spirkel, W. & Ries, H. (1995) *Phys. Rev. E Stat. Phys. Plasmas Fluids Relat. Interdiscip. Top.* **52**, 3485–3488.
- Weinhold, F. (1975) *J. Chem. Phys.* **63**, 2479–2483.
- Salamon, P., Nitzan, A., Andresen, B. & Berry, R. S. (1980) *Phys. Rev. A At. Mol. Phys.* **21**, 2115–2127.
- Diosi, L., Kulacsy, K., Lukacs, B. & Racz, A. (1996) *J. Chem. Phys.* **105**, 11220–11225.
- Eddington, A. S. (1923) *The Mathematical Theory of Relativity* (Cambridge Univ. Press, Cambridge, U.K.).
- Sears, F. W., Zemansky, M. W. & Young, H. D. (1987) *University Physics* (Addison-Wesley, Boston), p. 961.
- Enquist, B. J., West, G. B., Charnov, E. L. & Brown, J. H. (1999) *Nature (London)* **401**, 907–911.
- Calder, W. A. (1984) *Annu. Rev. Ecol. Syst.* **14**, 213–230.
- Aoki, I. (1989) *J. Theor. Biol.* **141**, 11–21.
- Salamon, P., Hoffmann, K. H., Schubert, S., Berry, R. S. & Andresen, B. (2001) *J. Non-Equilib. Thermodyn.* **26**, 73–83.
- Dodds, P. S., Rothman, D. H. & Weitz, J. S. (2001) *J. Theor. Biol.* **209**, 9–27.
- Charnov, E. L. (1993) *Life History Invariants: Some Explorations of Symmetry in Evolutionary Ecology* (Oxford Univ. Press, Oxford).